DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

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Date:

From: Interdisciplinary Scientist, Division of Dietary Supplement Programs , Office of Nutritional Products, Labeling and Dietary Supplements, HFS-810

Subject: 75-Day Premarket Notification of New Dietary Ingredients

To: Dockets Management Branch, HFA-305

Subject of the Notification:
Kaneka Glavanoid Rich Oil brand of Licorice Flavanoid Oil (LFO)

Firm: **Kaneka Corporation**

Date Received by FDA: **12/7/2004**

90-Day Date: **3/7/2005**

In accordance with the requirements of section 413(a) of the Federal Food, Drug, and Cosmetic Act, the attached 75-day premarket notification and related correspondence for the aforementioned substance should be placed on public display in docket number 95S-0316 as soon possible since it is past the 90-day date. Thank you for your assistance.

Linda Pellicore, Ph.D

19955-0316

RPT267

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
5100 Paint Branch Parkway
College Park, Maryland 20740

FEB 18 2005

David H. Bechtel, Ph.D.
Cantox Health Sciences International
1011 U.S. Highway 22 West, Suite 200
Bridgewater, NJ 08807-2950

Dear Dr. Bechtel:

This is to inform you that the notification you submitted, dated December 6, 2004, on behalf of your client, Kaneka Corporation, pursuant to 21 U.S.C. 350b(a)(2)(section 413(a)(2) of the Federal Food, Drug, and Cosmetic Act (the Act)) was filed by the Food and Drug Administration (FDA) on December 7, 2004. Your notification concerns the substance "Kaneka Glavonoid Rich Oil Brand of Licorice Flavanoid Oil (LFO)", prepared from *Glycyrrhiza glabra* L. that you intend to market as a new dietary ingredient.

According to the notification, you intend to market your new dietary ingredient "Kaneka Glavonoid Rich Oil Brand of Licorice Flavanoid Oil (LFO)" in capsule form. You state in the notification that "the LFO capsule will be clearly labeled and promoted as a dietary supplement. A description of the number of capsules per serving size will appear on the label, and each serving of the dietary supplement will contain 30 mg licorice ethanol extract (equivalent to approximately 300 mg LFO). Consumption of up to 2 servings per day will be suggested or recommended in the label directions, resulting in a maximum daily consumption of up to 60 mg licorice ethanol extract (equivalent to approximately 600 mg LFO, or 10 mg/kg/day for a 60 kg body weight person)."

Under 21 U.S.C. 350b(a), the manufacturer or distributor of a dietary supplement containing a new dietary ingredient that has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered must submit to FDA, at least 75 days before the dietary ingredient is introduced or delivered for introduction into interstate commerce, information that is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such new dietary ingredient will reasonably be expected to be safe. FDA reviews this information to determine whether it provides an adequate basis for such a conclusion. Under section 350b(a)(2), there must be a history of use or other evidence of safety establishing that the new dietary ingredient, when used under the conditions recommended or suggested in the labeling of the dietary supplement, will reasonably be expected to be safe. If this requirement is not met, the dietary supplement is considered to be adulterated under 21 U.S.C. 342(f)(1)(B) because there is inadequate information to provide reasonable assurance that the new dietary ingredient does not present a significant or unreasonable risk of illness or injury.

FDA has carefully considered the information in your submission, and the agency has concerns about the evidence on which you rely to support your conclusion that a dietary supplement containing "LFO" will reasonably be expected to be safe.

The product Licorice Flavonoid Oil (LFO) is an oil derived from the root of *Glycyrrhiza glabra*. Based on the information provided, the oil is an ethanol extract of licorice root. The product "LFO" is composed of 90% medium-chain triglycerides (MCT) and 10% licorice ethanol extract.

Glycyrrhizinic acid is said to be present at a concentration < 0.001%. This value appears to have been calculated from an estimate of the detection limit for glycyrrhizinic acid during HPLC analysis. Despite statements in the notification that the glycyrrhizinic acid content of "LFO" is < 0.001%, there is no specification for glycyrrhizinic acid.

Only the studies cited in Sections 4.2.1.1., 4.2.1.2. and 4.2.1.3. appear to have been conducted with the "LFO" product that is the subject of the notification. However, the description of the test material for the study described in Section 4.2.1.1. is ambiguous. It is not clear whether LFO concentrate solution or "LFO" itself was the test material.

The other studies cited in Sections 4.2.2. and 4.2.3. utilized test materials whose relationship(s) to the ingredient that is the subject of the notification are not stated.

It is unclear to FDA whether the test substances used in the referenced studies in section 4.2.2.1. and 4.2.2.2. are the same as the "LFO", in your notification. For example, in section 4.2.2.2 in a subacute toxicity study, the test material is described as a "water freeze-dried extract of *Glycyrrhiza glabra*". Therefore, it is not evident that the test substances used in the referenced studies are qualitatively or quantitatively similar to the "LFO", that is your proposed new dietary ingredient, or how these studies are relevant to evaluating the safe use of your proposed new dietary ingredient under the recommended conditions of use.

For the reasons discussed above, the information in your submission does not provide an adequate basis to conclude that "LFO" when used under the conditions recommended or suggested in the labeling of your product, will reasonably be expected to be safe. Therefore, your product may be adulterated under 21 U.S.C. 342(f)(1)(B) as a dietary supplement that contains a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such a product into interstate commerce is prohibited under 21 U.S.C. 331(a) and (v).

Your notification will be kept confidential for 90 days after the filing date of December 7, 2004. After the 90-day date, the notification will be placed on public display at FDA's Division of Docket Management in docket number 95S-0316. Prior to that date, you may wish to identify in writing specifically what information you believe is proprietary, trade secret or otherwise confidential for FDA's consideration.

If you have any questions concerning this matter, please contact Linda Pellicore, Ph.D at (301) 436-2375.

Sincerely yours,

Susan J. Walker, M.D.
Director
Division of Dietary Supplement Programs
Office of Nutritional Products, Labeling
and Dietary Supplements
Center for Food Safety
and Applied Nutrition

CANTOX
HEALTH SCIENCES INTERNATIONAL

1011 U.S. Hwy 22 West, Suite 200
Bridgewater, New Jersey 08807-2950
Phone: (908) 429-9202
Fax: (908) 429-9260

December 6, 2004

Office of Nutritional Products, Labeling, and Dietary Supplements (HFS-820)
Center for Food Safety and Applied Nutrition
Food and Drug Administration
5100 Paint Branch Pkwy
College Park, MD 20740

DEC 07 2004
CFSAN/FDA

RE: New Dietary Ingredient Notification

Dear Sir or Madam,

In accordance with the provisions of Section 413(a) of the Federal Food, Drug and Cosmetic Act, CANTOX U.S. Inc., on behalf of Kaneka Corporation, submits the attached information to the Food and Drug Administration, in support of marketing of a dietary supplement, containing the new dietary ingredient Kaneka Glavonoid Rich Oil™ brand of Licorice Flavonoid Oil (LFO). It is Kaneka Corporation's intention to incorporate the ingredient LFO into a dietary supplement in the form of capsules. Pursuant to the applicable provisions of the DSHEA, 21 U.S.C. § 350b (a) (2), Kaneka Corporation will not introduce the ingredient or deliver it for introduction into interstate commerce until at least 75 days after the date on which FDA receives this notification.

Respectfully submitted,

David H. Bechtel, Ph.D., DABT
Senior Scientific Consultant

Enclosure